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Original Article

Early Predictive Value of Peripheral Inflammatory Index Combined with High-Sensitivity Troponin T for Sepsis-Induced Cardiomyopathy

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Abstract. ***Background:*** **Sepsis-induced cardiomyopathy (SICM) is a common and serious complication of sepsis, and early identification remains challenging. Inflammatory and immune markers may provide complementary information to myocardial injury biomarkers.**

Methods**: A total of 319 adult patients with a first diagnosis of sepsis between June 2022 and January 2025 were enrolled. Complete blood counts and high-sensitivity cardiac troponin T (hs-cTnT) were collected within 0–6 hours after diagnosis. SICM was determined based on clinical and imaging data. Peripheral blood inflammatory indices (PBIIs), including NLR, SII, SIRI, PLR, and PIV, were calculated from blood counts. Variable robustness was assessed using LASSO logistic regression combined with bootstrap resampling. Univariate and multivariate logistic regression analyses were then performed to construct predictive models, and model performance was evaluated using ROC curves, calibration curves, and decision curve analysis.**

Results**: Among 319 patients with sepsis, 115 (36.1%) developed SICM. Compared with the non-SICM group, patients with SICM had significantly higher hs-cTnT levels, indicating more severe myocardial injury. Peripheral inflammatory indices were also higher overall, with the largest between-group differences observed for SII and NLR. SIRI and PLR were also elevated, whereas PIV showed a smaller difference (all P<0.05). The baseline model including hs-cTnT achieved an AUC of 0.825; adding SII or NLR further improved discrimination, with AUCs of 0.856 and 0.860, respectively. Calibration and decision curve analyses showed consistent model performance.**

Conclusion**: SII and NLR, as readily available peripheral inflammatory markers, were associated with improved early prediction of SICM when combined with hs-cTnT. This combined strategy may help refine early risk stratification in patients with sepsis.**

Keywords: Sepsis; Sepsis-induced cardiomyopathy; hs-cTnT; Systemic immune-inflammation index; Neutrophil-to-lymphocyte ratio; Early prediction.

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Introduction. Sepsis is a life-threatening syndrome characterized by infection-triggered systemic inflammation and immune dysregulation. It remains one of the leading causes of death among hospitalized patients and is particularly common in intensive care units[1,2]. Its hallmark is multiple organ dysfunction, and SICM represents an acute and potentially reversible form of cardiac dysfunction. SICM is characterized by acute left-sided or biventricular systolic and/or diastolic dysfunction unrelated to coronary artery disease, and it has a high incidence and is closely associated with increased mortality.[3] According to Sepsis-3, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.[4] Given its substantial global burden, early identification and intervention are essential to reduce mortality. The presence of SICM not only worsens tissue hypoxia and hypoperfusion but may also contribute to the progression of multiple organ dysfunction, making early prediction clinically important.[5]

The pathogenesis of SICM remains incompletely understood. Existing evidence suggests that inflammatory mediator release, oxidative stress, mitochondrial dysfunction, and metabolic disorders are central mechanisms.[5,6] During the progression of sepsis, dysregulated immune responses trigger the massive release of inflammatory mediators (e.g., TNF-α and IL-6), directly damaging cardiomyocytes and impairing contractile function.[7] Oxidative stress not only exacerbates inflammation but also disrupts mitochondrial energy metabolism, leading to impaired myocardial contraction and relaxation.[8] In addition, hemodynamic disturbances and inadequate microcirculatory perfusion may induce myocardial ischemia and further aggravate cardiac dysfunction.[9] Therefore, SICM is closely linked to disruption of the inflammatory microenvironment, and inflammatory markers may help reflect inflammatory severity and the risk of myocardial injury.[10]

In clinical research, hs-cTnT is a commonly used marker of myocardial injury and has been applied in the prediction of several infection-related cardiac conditions.[11-14] At the same time, peripheral blood inflammatory indices (PBIIs) derived from routine blood parameters have received increasing attention in recent years.[15,16] These indices are simple, low-cost, and widely available in routine practice. Commonly used indicators include the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and pan-immune-inflammation value (PIV). Existing studies suggest that these markers have predictive value in multiple diseases, but evidence supporting their use in sepsis, especially SICM, remains limited.[17-20]

Given the adverse impact of SICM on patient outcomes and the limitations of existing single inflammatory markers or myocardial injury indicators in clinical prediction, this study aimed to explore the early predictive value of hs-cTnT combined with PBIIs (SII, NLR, PLR, SIRI, and PIV) for identifying SICM in patients with sepsis, with the goal of providing a simple, accessible, and clinically practical predictive approach.

Methods.

Study population and inclusion and exclusion criteria. Adult patients (aged ≥18 years) who first met the definition of sepsis during hospitalization between June 2022 and January 2025 were included. The time point at which the criteria were first met was defined as t0. Participants were required to undergo a complete blood count and hs-cTnT testing within 0–6 hours after t0, and to have an interpretable transthoracic echocardiogram within 24–72 hours after t0. Key clinical data, including demographics, comorbidities, vital signs, therapeutic interventions, and organ function scores, were also required. Exclusion criteria were as follows: previously diagnosed structural or ischemic heart disease; acute coronary syndrome not ruled out or confirmed on admission; atrial fibrillation; failure to undergo blood count or hs-cTnT testing within 0–6 hours after t0, or absence of interpretable echocardiography within 24–72 hours; death within 24 hours of admission with unattainable outcome assessment; pregnancy or lactation; non-sepsis-related hospitalization; significant and uncorrectable volume overload; severe arrhythmia or pacemaker dependency; and significant immunosuppression. The study obtained ethical approval and used de-identified data.

Outcome assessment of Sepsis-3 and SICM. According to the Third International Consensus on Sepsis and Septic Shock,[20] Sepsis-3 is defined as organ dysfunction occurring in the context of, or with strong suspicion of, infection, with an operational criterion of a ≥2-point increase in the SOFA score from baseline. The time point at which this criterion was first met was defined as t0, which determined the time windows for laboratory sampling and ultrasound assessment in this study. The outcome was SICM, independently assessed by two qualified sonographers under blinded conditions. Discrepancies were resolved by a third expert, and cases with poor image quality were considered uninterpretable. SICM was diagnosed when any one of the following criteria was met: ① left ventricular ejection fraction (LVEF) <50% or a decrease of ≥10% from baseline; ② absolute global longitudinal strain (GLS) <16%; or ③ right ventricular dysfunction (TAPSE <17 mm or tricuspid annular S′ <10 cm/s).[21-23] Cases meeting these criteria were classified as SICM+, and the remainder as non-SICM. Echocardiographic assessments used for classification were limited to examinations performed within 24–72 hours after t0; when multiple examinations were available, the first interpretable result was used.

Clinical Data Collection and Variables. The first available value within the 0–24-hour window after t0 was extracted using a standardized template. Collected data included demographics and comorbidities (e.g., age, sex, and chronic disease history), vital signs and therapeutic support (e.g., blood pressure, heart rate, mechanical ventilation, and hemodynamic/device support), and organ function scores (e.g., SOFA). All information was obtained from routine hospital records, and ultrasound interpreters remained blinded to the clinical and laboratory data.

Laboratory and Parameter Calculation. Blood was collected within 0–6 hours after t0 according to hospital standard operating procedures, using either peripheral venipuncture or an indwelling venous catheter. Two milliliters of EDTA-K_2 anticoagulated whole blood were collected for complete blood count analysis on a Beckman Coulter hematology analyzer. In addition, 3–5 mL of blood was collected into a serum separator tube for immunological and biochemical assays (hs-cTnT, CRP, PCT, and IL-6). After complete coagulation, serum samples were centrifuged at 1,500 g for 10 minutes at room temperature, and testing and quality control were performed on the Beckman Coulter immunoassay platform according to the manufacturer's instructions. PBIIs were calculated from the concurrent complete blood count as follows: NLR = Neu/Lym, PLR = Plt/Lym, SII = (Plt×Neu)/Lym, SIRI = (Neu×Mon)/Lym, and PIV = (Neu×Plt×Mon)/Lym.

Statistical analysis. Statistical analyses were performed in R 4.4.3, using the main packages glmnet, pROC, rms, and rmda. Univariate logistic regression was first conducted for each candidate variable, and the associations with the outcome were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Candidate variables were then entered into multivariable logistic regression. The penalty parameter for LASSO regression (α=1) was selected by 10-fold cross-validation, with preference given to λ.1se. Stability was further assessed using bootstrap resampling (B=500). The final model was established on the basis of the screening results, and individual predicted probabilities were calculated.

Model discrimination was evaluated using ROC curves and the AUC with DeLong 95% CIs. Thresholds were determined using Youden's index, and the corresponding sensitivity, specificity, false-positive rate, false-negative rate, Youden's index, threshold value, and P value were reported. Calibration was assessed by comparing predicted probabilities with observed event rates across deciles; an apparent LOESS calibration curve (span=0.75) was plotted, bootstrap bias correction was performed with 500 resamples, and a Hosmer–Lemeshow test (g=10) was conducted. Decision curve analysis (DCA) was used to calculate net benefit across threshold probabilities from 0.05 to 0.95. All statistical tests were two-sided, and P<0.05 was considered statistically significant.

Results.

Baseline characteristics. This study enrolled 319 hospitalized patients with sepsis who met the inclusion criteria, including 115 patients (36.1%) in the SICM group and 204 in the non-SICM group (**Figure 1**). No statistically significant differences were observed between the two groups in age, sex, or BMI (all P>0.05). Regarding vital signs, the SICM group had lower systolic blood pressure (112±13 vs 115±13 mmHg, P=0.049) and diastolic blood pressure (62±8 vs 66±8 mmHg, P<0.001), whereas heart rate was similar between groups (93.8±11.1 vs 93.0±11.0 beats/min, P=0.502). With respect to hematologic and inflammatory markers, the SICM group had higher white blood cell and neutrophil counts, together with lower lymphocyte and monocyte counts (all *P*<0.001). C-reactive protein, procalcitonin, and IL-6 levels were also significantly higher (all *P*<0.001), whereas platelet counts did not differ significantly (P=0.749). Regarding therapeutic support, the SICM group more frequently received mechanical ventilation (41.7% vs 24.5%, P=0.002) and hemodynamic/mechanical circulatory support (20.0% vs 4.4%, P<0.001), with a trend toward a difference in renal replacement therapy (16.5% vs 8.8%, P=0.060). Among comorbidities, hypertension was more common in the SICM group (40.0% vs 27.5%, P=0.029), whereas chronic kidney disease and coronary heart disease did not differ significantly. The SICM group also had higher SOFA scores (9.34±1.18 vs 8.89±1.19, P=0.001) (**Table 1**).

Distribution of hs-cTnT and peripheral inflammatory immune markers stratified by SICM. Among the 319 patients with sepsis, those with SICM had significantly higher hs-cTnT levels than those without SICM (27.44 ± 4.99 vs 22.05 ± 5.10 ng/L, *P*<0.001), indicating more severe myocardial injury. Peripheral inflammatory immune indices were also generally higher in the SICM group: NLR was 4.82 [3.94, 6.21] vs 3.75 [3.19, 4.46] (*P*<0.001), SII was 996.50 [756.16, 1318.82] vs 674.63 [539.62, 870.17] (P<0.001), PLR was 128.65 [98.73, 166.59] vs 104.78 [83.29, 127.59] (*P*<0.001), SIRI was 2.26 [1.62, 2.88] vs 1.99 [1.42, 2.35] (*P*=0.001), and PIV was 435.94 [280.18, 595.86] vs 361.61 [267.88, 485.28] (*P*=0.016) (**Figure 2**). Among these indices, the between-group differences were most pronounced for

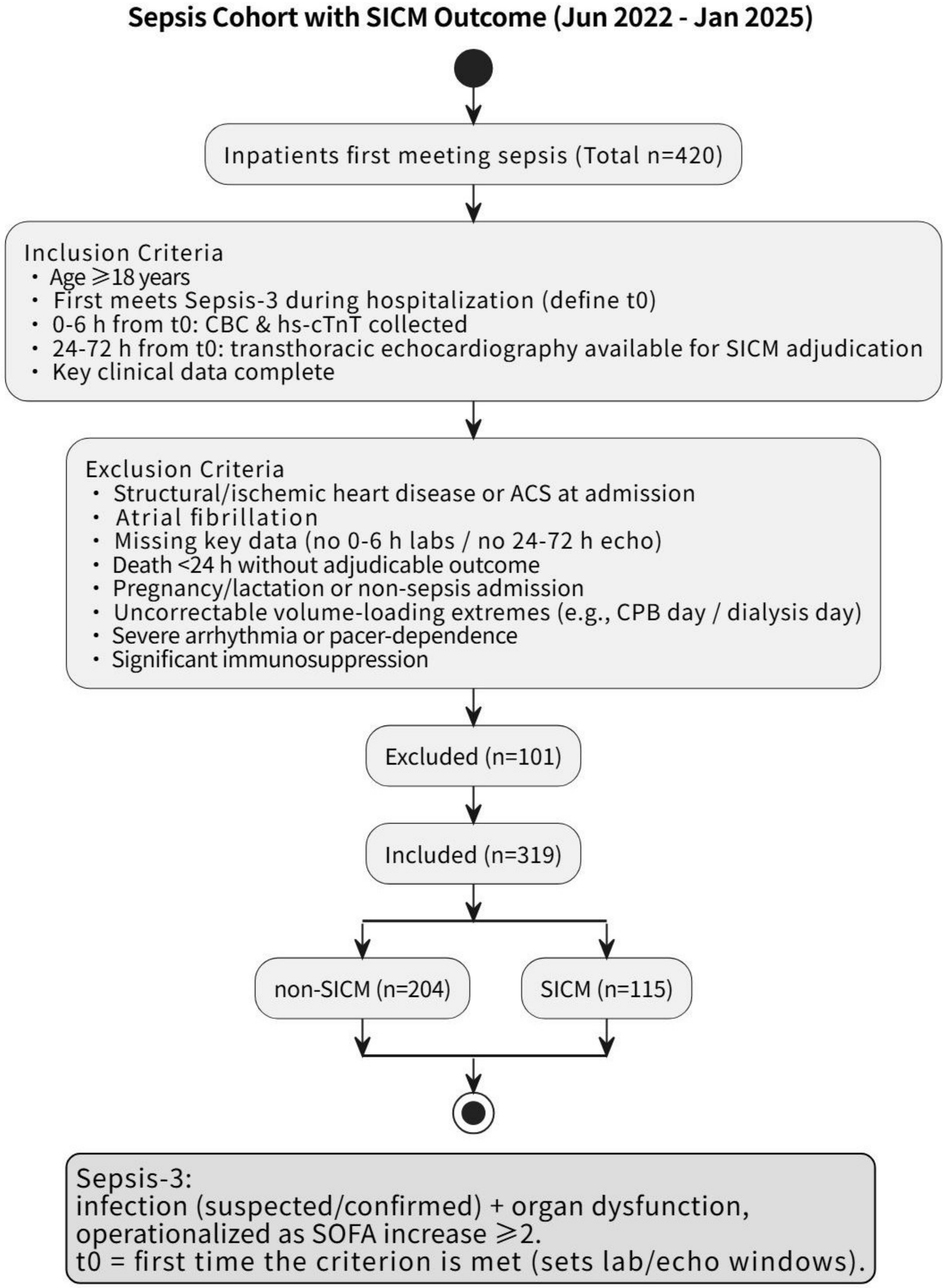


Figure 1. Study flow diagram for the sepsis cohort and SICM adjudication. Hospitalized adults first meeting Sepsis-3 (t0) were screened (Total n=420); inclusion required labs (CBC, hs-cTnT) within 0–6 h from t0 and transthoracic echocardiography within 24–72 h for SICM adjudication. After exclusions (n=101), 319 patients were included and classified as non-SICM (n=204) or SICM (n=115). Abbreviations: Sepsis-3, Third International Consensus; t0, first time Sepsis-3 criteria are met; hs-cTnT, high-sensitivity cardiac troponin T; CBC, complete blood count; SICM, sepsis-induced cardiomyopathy.

Table 1. Baseline characteristics of the study cohort stratified by SICM status.

Variables	Total (n=319)	non-SICM (n=204)	SICM (n=115)	*P* value
Demographics				
Age (years)	63.28 ± 11.77	63.41 ± 11.78	63.05 ± 11.80	0.792
Female sex, n (%)	147 (46.1%)	89 (43.6%)	58 (50.4%)	0.292
BMI (kg/m^2)	22.87 ± 2.67	22.94 ± 2.70	22.74 ± 2.63	0.516
SBP (mmHg)	113.92 ± 13.06	115.00 ± 13.00	112.00 ± 13.00	0.049
DBP (mmHg)	64.56 ± 8.21	66.00 ± 7.99	62.00 ± 8.00	<0.001
HR (beats/min)	93.27 ± 11.01	92.95 ± 10.98	93.82 ± 11.09	0.502
Laboratory tests				
WBC ($\times10^9$/L)	10.54 ± 2.92	9.86 ± 2.35	11.76 ± 3.41	<0.001
Neu ($\times10^9$/L)	7.09 ± 1.49	6.67 ± 1.30	7.83 ± 1.51	<0.001
Lym ($\times10^9$/L)	1.79 ± 0.49	1.90 ± 0.45	1.58 ± 0.48	<0.001
Mon ($\times10^9$/L)	0.51 ± 0.14	0.54 ± 0.14	0.44 ± 0.12	<0.001
Platelets ($\times10^9$/L)	197.86 ± 48.60	197.18 ± 46.07	199.07 ± 52.98	0.749
CRP (mg/L)	42.08 ± 11.31	37.71 ± 8.85	49.82 ± 11.07	<0.001
PCT (ng/L)	1.57 ± 0.37	1.52 ± 0.36	1.67 ± 0.35	<0.001
IL-6 (pg/mL)	0.45 ± 0.11	0.44 ± 0.08	0.47 ± 0.15	0.044
Treatment/Support				
Mechanical ventilation, n (%)	98 (30.7%)	50 (24.5%)	48 (41.7%)	0.002
Renal replacement therapy, n (%)	37 (11.6%)	18 (8.8%)	19 (16.5%)	0.060
Heart support, n (%)	32 (10.0%)	9 (4.4%)	23 (20.0%)	<0.001
Comorbidities				
Hypertension, n (%)	102 (32.0%)	56 (27.5%)	46 (40.0%)	0.029
Diabetes, n (%)	78 (24.5%)	53 (26.0%)	25 (21.7%)	0.477
Chronic kidney disease, n (%)	108 (33.9%)	62 (30.4%)	46 (40.0%)	0.106
Coronary artery disease, n (%)	33 (10.3%)	20 (9.8%)	13 (11.3%)	0.817
SOFA (points)	9.05 ± 1.20	8.89 ± 1.19	9.34 ± 1.18	0.001

Data are presented as mean ± SD for continuous variables and n (%) for categorical variables. P values were obtained using Student's t test (or Wilcoxon rank-sum test where appropriate) for continuous variables and χ^2 (or Fisher's exact) test for categorical variables. Units: SBP/DBP, mmHg; HR, beats per minute (bpm); SOFA, points. Statistical significance set at P<0.05.
Abbreviations: SICM, sepsis-induced cardiomyopathy; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; WBC, white blood cell count; Neu, neutrophils; Lym, lymphocytes; Mon, monocytes; CRP, C-reactive protein; PCT, procalcitonin; IL-6, interleukin-6; MV, mechanical ventilation; RRT, renal replacement therapy; CKD, chronic kidney disease; CAD, coronary artery disease; BMI, body mass index.

SII and NLR, whereas the differences for SIRI and PIV were smaller but still statistically significant. Overall, these findings suggest that patients with SICM exhibit more marked abnormalities in both myocardial injury markers and inflammation-related indices.

Correlation between hs-cTnT and PBII. Spearman correlation analysis showed that hs-cTnT was weakly correlated with the peripheral inflammatory indices (ρ=0.11–0.24). Specifically, the correlation coefficient was 0.22 with NLR (*P*<0.001), 0.19 with PLR (P<0.001), 0.24 with SII (*P*<0.001), and 0.11 with PIV (*P*<0.05), whereas the correlation with SIRI was not statistically significant (ρ=0.11, $P\geq0.05$). In contrast, significant and strong positive correlations were observed among the inflammatory indices themselves. For example, the correlation coefficient was 0.87 between PIV and SIRI (P<0.001), 0.86 between PLR and SII (P<0.001), 0.80 between SII and PIV (P<0.001), 0.68 between NLR and SII (P<0.001), and 0.66 between NLR and SIRI (P<0.001). These results indicate substantial collinearity among the inflammatory indices, whereas hs-cTnT shows only weak positive correlations with PBII (**Figure 3**).

LASSO-Based Variable Selection and Stability Assessment. For variable selection, hs-cTnT, the various PBIIs, and clinical covariates were entered into LASSO logistic regression. The penalty parameter was selected using 10-fold cross-validation, and stability was further assessed with 500 bootstrap resamples (**Figure 4**). Variables with a stable selection frequency of at least

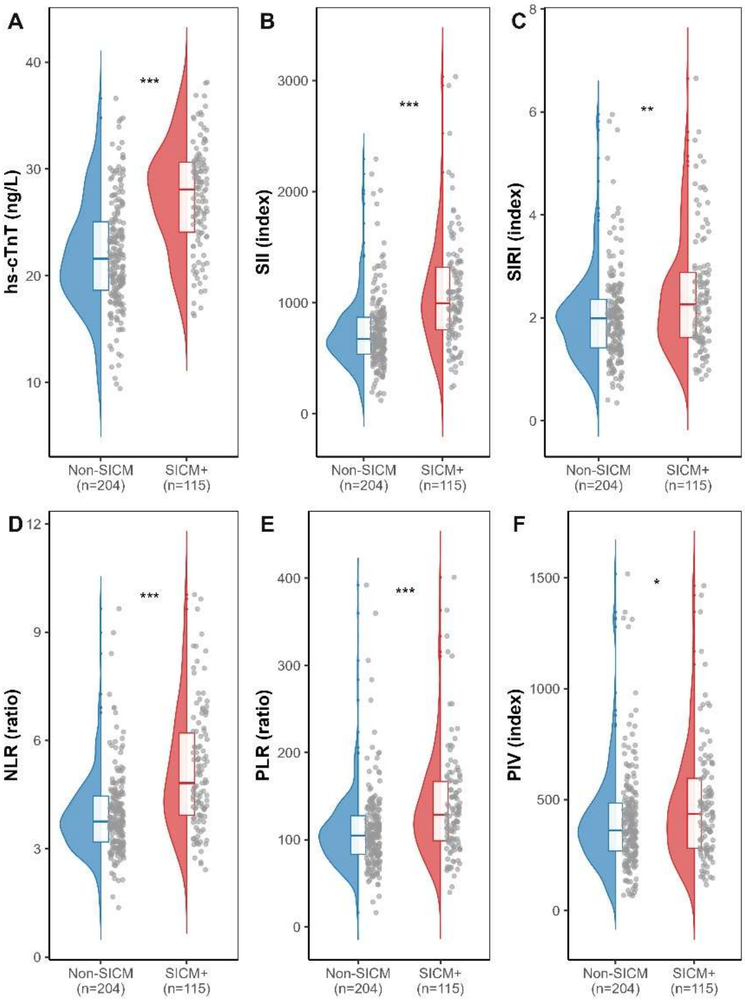
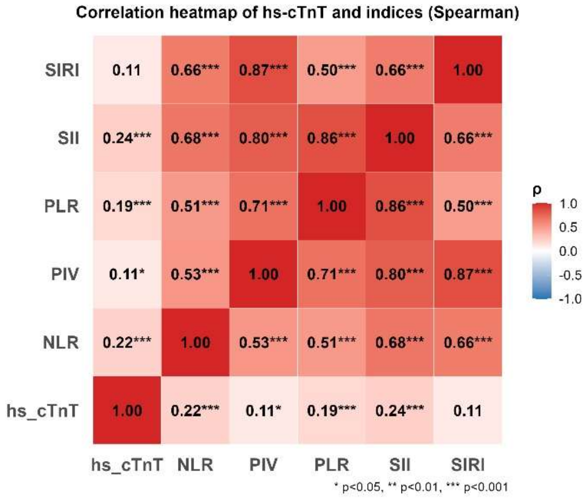


Figure 2. Distributions of hs-cTnT and peripheral blood inflammatory indices by SICM status. Violin plots with overlaid box-and-whisker plots (median and IQR) and jittered points compare non-SICM (n=204) with SICM+ (n=115) for (A) hs-cTnT (ng/L), (B) SII (index), (C) SIRI (index), (D) NLR (ratio), (E) PLR (ratio), and (F) PIV (index). P values were obtained using Welch's t-test for hs-cTnT and Wilcoxon rank-sum tests for PBII because of skewed distributions; significance codes: P<0.05 (*), P<0.01 (**), and P<0.001 (***). Abbreviations: SICM, sepsis-induced cardiomyopathy; hs-cTnT, high-sensitivity cardiac troponin T; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; PIV, pan-immune-inflammation value.


Correlation heatmap of hs-cTnT and indices (Spearman)

	hs_cTnT	NLR	PIV	PLR	SII	SIRI
SIRI	0.11	0.66***	0.87***	0.50***	0.66***	1.00
SII	0.24***	0.68***	0.80***	0.86***	1.00	0.66***
PLR	0.19***	0.51***	0.71***	1.00	0.86***	0.50***
PIV	0.11*	0.53***	1.00	0.71***	0.80***	0.87***
NLR	0.22***	1.00	0.53***	0.51***	0.68***	0.66***
hs_cTnT	1.00	0.22***	0.11*	0.19***	0.24***	0.11

Figure 3. Spearman correlation heatmap of hs-cTnT and peripheral blood inflammatory indices (PBII).
Heatmap of pairwise Spearman correlation coefficients (ρ) among hs-cTnT and PBII (NLR, PLR, SII, SIRI, PIV). Numeric ρ values are printed in each tile; color encodes the magnitude (−1 to 1). Significance: P<0.05 (*), P<0.01 (**), P<0.001 (***).

70% included hs-cTnT, SII, NLR, PIV, SOFA, systolic blood pressure, hemodynamic/mechanical circulatory support, and mechanical ventilation. Among these, hs-cTnT had a selection frequency of 100%, SII 99.4%, NLR 98.4%, PIV 96.2%, SOFA 97.6%, systolic blood pressure 91.2%, cardiac support 99.4%, and mechanical ventilation 76.6%. These findings suggest robust predictive contributions from myocardial injury markers, inflammatory indices, disease severity scores, and support-related variables for SICM prediction.

hs-cTnT Combined with elevated PBII for SICM discrimination and calibration. In multivariable logistic regression analysis, hs-cTnT remained an independent predictor, and after the addition of PBII, both SII and NLR also remained independently associated with SICM, whereas PIV did not (**Table 2**). In terms of discriminative performance, the AUC of the baseline model M0 (hs-cTnT, adjusted for Heart support, SOFA,

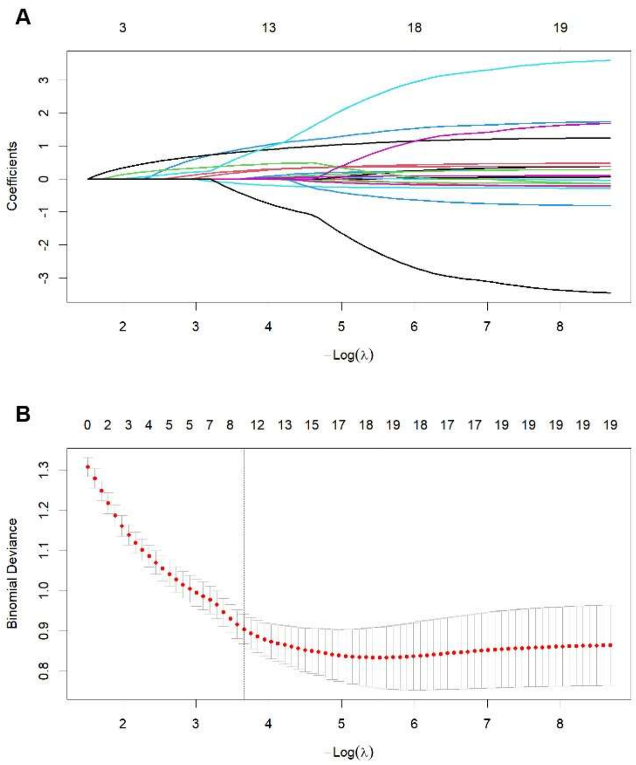


Figure 4. LASSO coefficient paths and cross-validated deviance for λ selection.
(**A**) Coefficient trajectories of candidate predictors across the regularization path (−log λ).
(**B**) Ten-fold cross-validated binomial deviance; vertical dotted lines indicate λ.min and λ.1se chosen for model selection.

MV, and SBP) was 0.825 (95% CI 0.778–0.871). After incorporating PBII, the AUC increased to 0.856 for M1 (hs-cTnT + SII; 95% CI 0.815–0.898, DeLong P=0.009) and to 0.860 for M2 (hs-cTnT + NLR; 95% CI 0.819–0.901, P=0.008), both significantly higher than M0. By contrast, M3 (hs-cTnT + PIV) had an AUC of 0.826 (95% CI 0.780–0.872), which was similar to M0 (P=0.694) (**Figure 5A**, **Table 3**). At the optimal Youden threshold, M1 and M2 showed higher Youden indices than M0 (approximately 0.57 vs 0.52), with improved specificity while maintaining high sensitivity. M1 showed a greater gain in sensitivity, whereas M2 showed a greater gain in specificity. Decision curve analysis showed that, across threshold probabilities of 0.05–0.95, M1 and M2 generally provided higher net benefit than the treat-all and treat-none strategies, particularly within the clinically relevant range of 0.10–0.60 (**Figure 5B**). Calibration plots showed that the apparent and bias-corrected curves of M1 and M2 were generally close to the ideal 45° line. Agreement between predicted and observed probabilities was good in the low- to medium-risk range. Although slight deviation was observed at the high-risk end, this was attenuated after bias correction, with no clear evidence of systematic over- or under-prediction (**Figure 5C–D**). Overall, adding SII or NLR to hs-cTnT improved model discrimination while preserving acceptable calibration, whereas PIV provided limited incremental value.

Discussion. Previous studies have consistently shown that SICM is a common complication of sepsis and is closely associated with adverse outcomes. Reported incidence rates range from approximately 20% to 43%. The incidence observed in the present study was 36.1%, which is broadly consistent with previous reports.[24-27] The development of SICM not only aggravates circulatory dysfunction but may also contribute to the progression of multiple organ failure. Accordingly, early prediction remains an important challenge in critical care medicine.

Traditional studies have largely focused on single biomarkers, including myocardial injury markers such as troponin and inflammatory markers such as CRP, PCT, and IL-6. Although these indicators can partly reflect myocardial injury or systemic inflammation, their predictive value is still limited when used alone. For example, one study reported that elevated cardiac troponin I (cTnI) was an independent predictor of short-term mortality in patients with septic shock, but its standalone accuracy was insufficient.[28] Another study found that combining blood glucose with hs-cTnT/I improved early risk identification in acute myocardial infarction, but the incremental diagnostic gain over hs-cTn alone was limited.[29] In patients with sepsis, admission hs-cTnT levels were significantly associated with 30-day and 1-year mortality, and among acute-phase survivors, hs-cTnT also remained predictive of mortality from 30 to 365 days.[30] In addition, some studies have suggested that although cTnI, CRP, and NLR are independent risk factors, their individual predictive performance is modest, supporting the rationale for combined assessment.[31]

In recent years, PBIIs have attracted increasing attention. These indices are derived from routine blood count parameters and have the advantages of simplicity, low cost, and high accessibility, while also reflecting inflammatory burden and immune status. Existing studies suggest that NLR, SII, PLR, SIRI, and PIV all have clinical value across multiple diseases.[17-20,32,33] Among them, NLR and SII are thought to better capture inflammatory burden and immune dysregulation. Multiple studies have confirmed their association with infection-related adverse outcomes, providing theoretical support for their use in sepsis-associated myocardial injury.[34,35]

NLR has accumulated substantial supporting evidence in sepsis populations. Ni et al. reported in an emergency department cohort that admission NLR was significantly associated with in-hospital mortality.[36] Li et al. analyzed the MIMIC-IV database and found that elevated NLR levels were independently associated with 28-day all-cause mortality in sepsis patients with

Table 2. Univariable and multivariable logistic regression across models (M0–M3).

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	aOR	95% CI	*P*
M0：hs-cTnT						
hs-cTnT	1.224	1.160–1.292	<0.001	1.234	1.165–1.306	<0.001
Heart support	5.417	2.411–12.170	<0.001	4.815	1.862–2.450	0.001
SOFA	1.385	1.133–1.692	0.001	1.411	1.113–1.789	0.004
MV	2.207	1.353–3.598	0.002	1.901	1.054–3.430	0.033
SBP	0.982	0.965–1.000	0.050	0.970	0.949–0.990	0.004
M1：hs-cTnT+SII						
hs-cTnT	1.224	1.160–1.292	<0.001	1.210	1.140–1.285	<0.001
SII	1.002	1.001–1.003	<0.001	1.002	1.001–1.003	<0.001
Heart support	5.417	2.411–12.170	<0.001	4.803	1.818–12.688	0.002
SOFA	1.385	1.133–1.692	0.001	1.480	1.155–1.897	0.002
MV	2.207	1.353–3.598	0.002	1.831	0.978–3.429	0.059
SBP	0.982	0.965–1.000	0.050	0.974	0.953–0.996	0.019
M2：hs-cTnT+NLR						
hs-cTnT	1.224	1.160–1.292	<0.001	1.221	1.148–1.298	<0.001
NLR	1.871	1.536–2.278	<0.001	1.761	1.403–2.212	<0.001
Heart support	5.417	2.411–12.170	<0.001	4.123	1.535–11.074	0.005
SOFA	1.385	1.133–1.692	0.001	1.510	1.174–1.941	0.001
MV	2.207	1.353–3.598	0.002	1.834	0.980–3.433	0.058
SBP	0.982	0.965–1.000	0.050	0.972	0.950–0.993	0.011
M3：hs-cTnT+PIV						
hs-cTnT	1.224	1.160–1.292	<0.001	1.228	1.159–1.301	<0.001
PIV	1.001	1.000–1.002	0.019	1.000	0.999–1.002	0.385
Heart support	5.417	2.411–12.170	<0.001	4.759	1.843–12.287	0.001
SOFA	1.385	1.133–1.692	0.001	1.424	1.122–1.808	0.004
MV	2.207	1.353–3.598	0.002	1.885	1.043–3.409	0.036
SBP	0.982	0.965–1.000	0.050	0.970	0.950–0.991	0.005

aOR = adjusted odds ratio. Adjusted models include Heart support, SOFA, mechanical ventilation (MV), and systolic blood pressure (SBP). Continuous variables were modeled on their original scales (hs-cTnT, ng/L; SII/PIV, index; NLR, ratio; SBP, mmHg; SOFA, points); binary variables coded 1 vs 0. Two-sided tests. Statistical significance set at P<0.05.

Abbreviations: hs-cTnT, high-sensitivity cardiac troponin-T; SII, systemic immune-inflammation index; NLR, neutrophil-to-lymphocyte ratio; PIV, pan-immune-inflammation value; SOFA, Sequential Organ Failure Assessment; SBP, systolic blood pressure; MV, mechanical ventilation; Heart support, hemodynamic/device support.

concomitant coronary artery disease.[37] Zhang et al. further showed in a large database study that the time-weighted average NLR was nonlinearly associated with 90-day in-hospital mortality, suggesting potential value for dynamic monitoring.[38] In studies of septic cardiomyopathy, Lan et al. identified NLR as an independent risk factor, and its diagnostic performance improved when combined with CRP and PLR.[31]

Research on SII is also expanding. Ou et al. found in patients with bloodstream infections that both SII and NLR were significantly associated with mortality risk, with nonlinear effects.[34] A review by Islam et al. emphasized the stability and reproducibility of SII and NLR under infectious stress conditions.[35] A meta-analysis of nine cohorts showed that high admission SII was associated with increased short-term mortality in sepsis.[40] Mangalesh et al. further suggested that combining SII with the SOFA score may improve mortality risk prediction in sepsis.[41] Chen et al. reported a U-shaped association between SII and hypertension risk in the NHANES cohort,[39] which, although outside the sepsis setting, supports the broader biological relevance of SII.

Overall, both NLR and SII can reflect inflammatory burden and immune dysregulation to some extent, and both show potential value for risk assessment in sepsis and its complications. On this basis, the present study further combined NLR and SII with hs-cTnT to evaluate their potential for early identification of SICM. The results showed that hs-cTnT levels were markedly

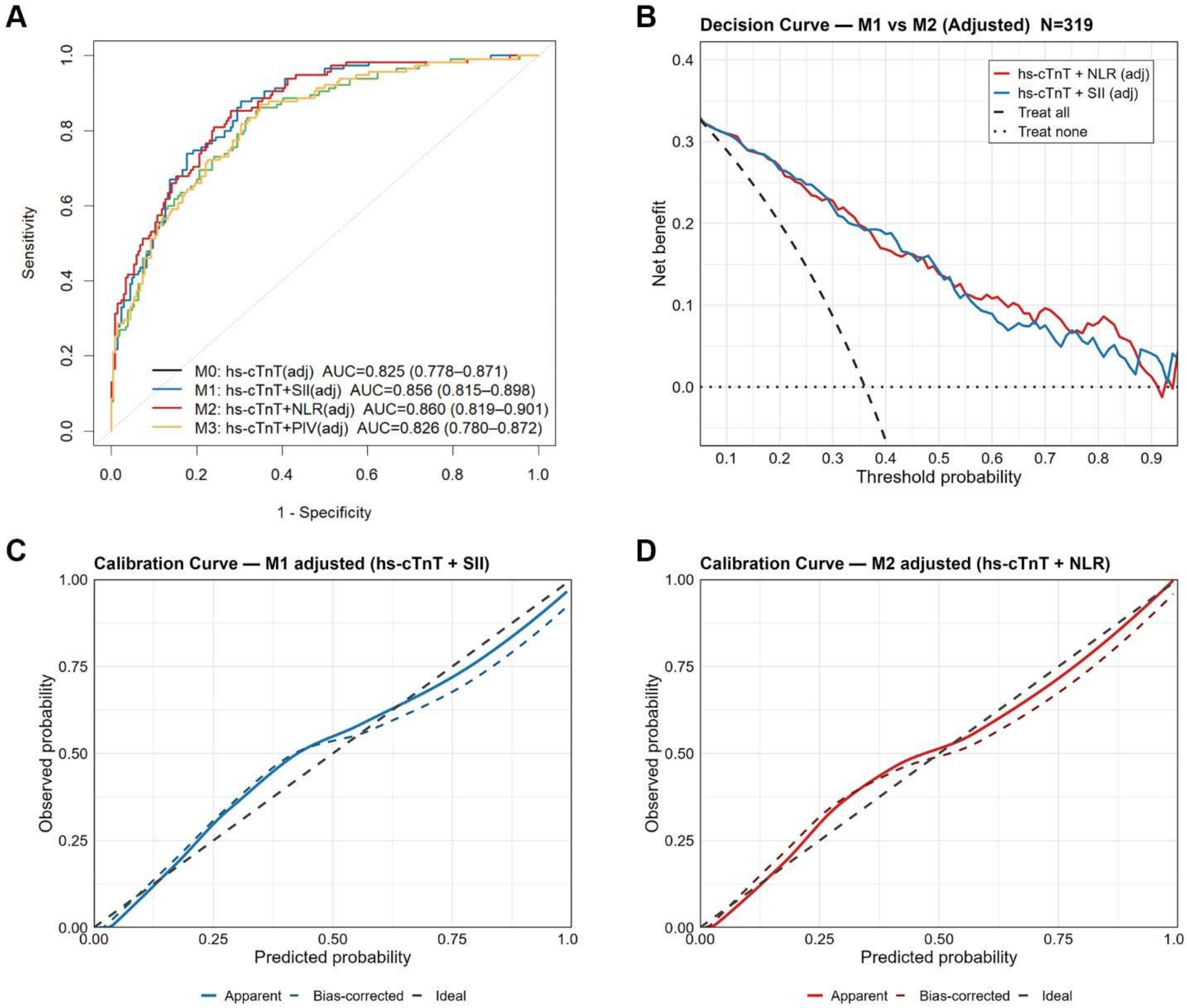


Figure 5. Discrimination, decision curve analysis, and calibration of adjusted models.
(**A**) ROC curves for M0–M3 with AUCs (DeLong 95% CIs); x-axis shows 1 − Specificity.
(**B**) Decision curve analysis comparing M1 (hs-cTnT + SII) and M2 (hs-cTnT + NLR) against "treat-all" and "treat-none" across a threshold range of 0.05–0.95 (step 0.01); N=319.
(**C–D**) Calibration of M1 (blue) and M2 (red): apparent LOESS curves and bias-corrected curves from out-of-bag bootstrap (B=500), with the 45° ideal reference.

elevated in patients with SICM, indicating more severe myocardial injury. Multiple PBIIs were also elevated, supporting the involvement of inflammatory burden and immune dysregulation in this condition. Among these indices, SII and NLR showed the most pronounced between-group differences. When combined with hs-cTnT in multivariable models, both markers improved discrimination, maintained acceptable calibration, and yielded more favorable net benefit on decision curve analysis. These findings support the complementary roles of inflammatory and myocardial injury markers in early SICM risk assessment. Similarly, Lan et al. reported that the combination of NLR, CRP, and PLR achieved good predictive accuracy for SICM, further supporting the value of multi-marker integration.[31]

It should also be noted that previous studies of NLR and SII have mainly focused on mortality or longer-term prognosis in sepsis,[34-40] and this body of evidence provides an important background for their application in critically ill populations. However, compared with mortality, SICM is a more proximal and potentially reversible complication. Earlier recognition of patients at higher risk of SICM may facilitate closer monitoring and timely supportive management. From this perspective, evaluating these inflammatory markers during the early phase of SICM may be more clinically informative than using them only for mortality stratification. In this context, the present findings suggest that combining hs-cTnT with either NLR or SII may provide a practical approach for early SICM risk assessment. Future studies should validate these findings in larger multicenter cohorts and determine whether the combined biomarker strategy remains informative in other inflammation-related cardiovascular settings. Exploratory questions may include conditions such as restenosis, post-cardiac inflammatory syndromes, including Dressler's syndrome, or treatment contexts involving biologic drugs. These extensions remain speculative and require dedicated prospective evaluation.

Conclusions. This study shows that combining hs-cTnT with PBIIs, particularly SII and NLR, may improve early risk assessment for SICM in patients with sepsis. Compared with single markers, these combined models showed better discrimination together with acceptable calibration and decision-curve performance. Because these markers are derived from routine laboratory tests, they are easy to obtain and may have practical value. Further validation in larger, multicenter cohorts is still needed. Integration with cardiac imaging and other multimodal approaches may provide a more robust basis for the early identification of sepsis-associated cardiomyopathy.

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Data available. Data is available from the corresponding author on request.

Ethics statement. All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by Nantong First People's Hospital.

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